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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,151	10/10/2003	Paul E. Segall	BIOT-005CON	2308

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	**Application No.** 10/684,151	**Applicant(s)** SEGALL ET AL.	
	Examiner Brian S. Kwon	**Art Unit** 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-37 and 39-51* is/are pending in the application.

4a) Of the above claim(s) _ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-37 and 39-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application

1. By Amendment filed 12/26/06, claims 31, 36, 41 and 49 have been amended. Claims 31-37 and 39-51 are currently pending for prosecution on the merits.

Summary of Action

2. The objection of claims 36 and 37 is not maintained in light of the amendment.

3. The rejection of claims 32-37, 39-41, 46-47 and 49 under 35 USC 112, second paragraph, is not maintained in light of the amendment.

4. The rejection of claims 31-37, 39-40, 41-44, 46-47 and 51 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 9 and 17 of U.S. Patent No. USP 6627393 is not maintained in light of the Approved Terminal Disclaimer filed 01/18/2007.

4. The rejection of claims 31-37 and 39-51 under 35 USC 103(a) as being unpatentable over either Segall et al. (WO 92/18136) in view of Irikura et al. (US 3937821), and further in view of Altura et al. ("Ca2+ coupling in vascular smooth muscle: Mg2+ and buffer effects on contractility and membrane Ca2+ movements", Canadian Journal of Physiology and Pharmacology, 1982, 60(4) 459-82) is maintained for the reasons of record.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 31-37 and 39-51 are rejected under 35 USC 103(a) as being unpatentable over either Segall et al. (WO 92/18136) in view of Irikura et al. (US 3937821), and further in view of Altura et al. ("Ca2+ coupling in vascular smooth muscle: Mg2+ and buffer effects on contractility and membrane Ca2+ movements", Canadian Journal of Physiology and Pharmacology, 1982, 60(4) 459-82).

The amended claims now read on a method of administering a composition comprising a physiologically acceptable aqueous solution comprising electrolytes, a dynamic buffering system such as a carboxylic acid, salt or ester thereof and an oncotic agent such hydroxethyl starch or dextran, further wherein said solution does not comprise a biological buffer, to a patient in a hyperbaric oxygen chamber (claims 31-37 and 39-41) or replacing a subject's circulating blood volume with said composition (claims 42-51) Further limitations include "said first and second oncotic agents have different molecular weight" (claim 32); "said first oncotic agent is a low to medium molecular weight onctoic agent and said second oncotic agent is a high molecular weight oncotic agent" (claim 33); "said first and second oncotic agent are polysaccharides" (claim 34); "hydroxethyl starches" (claim 35); "clearance rates differ by about 2 fold" (claim 36); "said first oncotic agent has a clearance rate of 2 to 3 hours and said second oncotic agent has a clearance rate of 6 hours" (claim 37); "carboxylic acid, salt, or ester thereof is selected from the group consisting of lactate, acetate, gluconate, citrate and pyruvate" (claims 39 and 50); "said dynamic buffering system further comprises bicarbonate" (claim 40); "a second onctoic agent whrein said second oncotic agent is a hydroxyethyl starch or dextran and wherein said first oncotic agent and second oncotic agent have differential clearing rates" (claim 41); "said subject is in a pressurized atmosphere of increased oxygen concentration, wherein said oxygen concentration is greater than 20 % oxygen" (claim 43); "said oxygen concentration is 100% oxygen" (claim 44); "said subject is in a hyperbaric chamber at hyperbaric pressures of about 0.07 to about 2 atmospheres over ambient pressure" (claim 45); "said subject's body temperature is maintained at a normal temperature" (claim 46); "said subject's body temperature is chilled to below normal temperature" (claim 47); "at least one cardioplegic agent, whererin said cardioplegic agent is lidocaine, procaine or novocaine" (claim 48); "said solution is augmented by adding an adduct and wherein said adduct is propanediol or high concentration glucose" (claim 49); and "said electrolytes comprises Na+, Cl-, Ca++, K+ and Mg++" (claim 51).

Segall (WO 92/18136) teaches a blood substitute composition comprising electrolytes (e.g., sodium, magnesium, chloride, calcium, potassium), glucose, carboxylic acid salt (e.g., sodium gluconate), two or more oncotic agents (e.g., high molecular hydroxyethyl starch, low molecular hydrxyethyl starch, dextran 40 and dextran 70) and biological buffer (e.g., TRIS, HEPES, TES, MOPS, TAPSO, EPPS). See page 8, line 15 thru page 20, line 32, Examples and Claims. The reference also teaches (i) the use of mixtures of carboxylic acid salt (e.g., sodium citrate, sodium gluconate, sodium pyruvate, sodium succinate, sodium bicarbonate and sodium lactate) in said composition (page 7, line 31 thru page 10, line 11); (ii) the use of simple hexose sugar (e.g., glucose, fructose and galactose) in the range of upto about 50nM, preferably in the range between 2 mM and 10mM (page 10, lines 9-24); (iii) the method of perfusing a subject prepared for circulatory perfusion (claim 41 and 45) whereby positioning said patient in a hyperbaric oxygen chamber at normal body temperatures and hyperbaric pressures of about 0.07 to about 2 atmospheres over ambient pressure (page 13, lines 13-16; page 16, lines 23-31; page 17, lines 7-11; Examples 4 and 7); (iv) the administration of said solution intravenously or intraarterially to an euthermic subject which is placed in a pressurized atmosphere of increased oxygen concentration exceeding 30%, preferably 50% or above up to 100% oxygen or to such a subject undergoing a procedure during which the subject's body temperature is reduced significantly below the subjects normal temperature (page 13, line 13 thru page 14, line 1; page 16, lines 23-31); (v) the administration of cardioplegic agents such as lidocaine, procaine and novocaine (page 14, lines 1-18); and the addition of adducts such as propanediol or between 0.6M to about 1.4M concentration of glucose to the solution (page 18, line 23 thru page 19, line 19).

Irikura teaches an aqueous-substitute solution which comprises one of various water-soluble hydroxyehtyl starches (having various degrees of substitutions, respectively) therein, wherein the solution does not include a biological buffer, comprises sodium lactate, as well as sodium chloride, potassium chloride, calcium chloride dehydrate and glucose (see entire documents, particularly Figures, Abstracts, Examples and Claims).

Altura teaches or suggests the disadvantage of using conventional buffers (e.g., TRIS, HEPES, MOPS, PIPES and bicine) in physiological solution because they can exert adverse effects on contractility and reactivity of certain arterial and venous smooth muscles.

The claimed invention differs from the references (Segall WO 92/18136) in the exclusion of conventional buffer and plurality of oncotic agents having differential clearance rates. To incorporate such teaching into the teaching of Segall (WO 92/18136), would have been obvious in view of Irikura who teaches an aqueous-substitute solution which comprises one of various water-soluble hydroxyehtyl starches, wherein the solution does not include a biological buffer, comprises sodium lactate, as well as sodium chloride, potassium chloride, calcium chloride dehydrate and glucose and further in view of Altura who teaches or suggests the disadvantage of using the conventional buffers in physiological solution.

It would have been obvious to one of ordinary skill in the art at the time of the invention was made to prepare blood substitute containing electrolytes, carboxylic acids such as hydroxyethyl starches or dextrans (having different clearance rates) without the presence of biological buffer and arrive at the claimed method in light of the cited references in combination. One having ordinary skill in the art would have been motivated to modify the teaching of Segall (WO 92/18136) such that the adverse effects associated with the use of conventional buffer such as TRIS, HEPES, MOPS and PIPES in said composition would be greatly eliminated. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Response to Arguments

6. Applicant's arguments filed 12/26/06 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that one of skill in the art reading Segall et al. would understand that the solution requires a biological buffer in order to maintain a proper pH. Applicant alleges that a skilled artisan would not be motivated to modify Segall's solution to exclude a biological buffer because Segall teaches away from a solution that excludes a biological buffer and the proposed modification would render Segall's solution unsatisfactory for its intended purpose.

This argument is not found persuasive. Unlike the applicant, the skill artisan would have expected as taught by Irikura and Altura that Segall's solution could be formulated without the convention buffers such as TRIS, HEPES, MOPS and PIPES (agents that are known to cause the adverse effects) and adjusted to appropriate pH (7.0-7.4) with other known buffering agent such as sodium bicarbonate (Examples of USP'821) that is included in Segall's solution (page 8, lines 10-11). One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
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